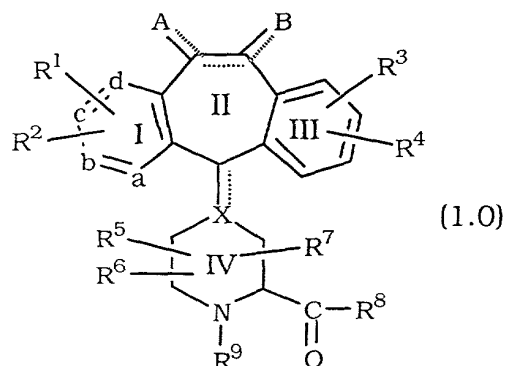


WHAT IS CLAIMED IS:

1. A compound of the formula:



or a pharmaceutically acceptable salt or solvate thereof, wherein:

- 5 one of a, b, c and d represents N or N'O', and the remaining a, b, c and d groups represent CR<sup>1</sup> or CR<sup>2</sup>; or

each of a, b, c, and d are independently selected from CR<sup>1</sup> or CR<sup>2</sup>;

- each R<sup>1</sup> and each R<sup>2</sup> is independently selected from H, halo,
- 10 -CF<sub>3</sub>, -OR<sup>10</sup>, -COR<sup>10</sup>, -SR<sup>10</sup>, -S(O)<sub>t</sub>R<sup>11</sup> (wherein t is 0, 1 or 2),  
-N(R<sup>10</sup>)<sub>2</sub>, -NO<sub>2</sub>, -OC(O)R<sup>10</sup>, -CO<sub>2</sub>R<sup>10</sup>, -OCO<sub>2</sub>R<sup>11</sup>, -CN,  
-NR<sup>10</sup>COOR<sup>11</sup>, -SR<sup>11</sup>C(O)OR<sup>11</sup>, -SR<sup>11</sup>N(R<sup>75</sup>)<sub>2</sub> (provided that R<sup>11</sup> in  
-SR<sup>11</sup>N(R<sup>75</sup>)<sub>2</sub> is not -CH<sub>2</sub>-) wherein each R<sup>75</sup> is independently  
selected from H or -C(O)OR<sup>11</sup>, benzotriazol-1-yloxy, tetrazol-5-  
15 ylthio, or substituted tetrazol-5-ylthio, alkynyl, alkenyl or alkyl, said  
alkyl or alkenyl group optionally being substituted with halo, -OR<sup>10</sup>  
or -CO<sub>2</sub>R<sup>10</sup>;

- R<sup>3</sup> and R<sup>4</sup> are the same or different and each independently  
represents H, any of the substituents of R<sup>1</sup> and R<sup>2</sup>, or R<sup>3</sup> and R<sup>4</sup>  
20 taken together represent a saturated or unsaturated C<sub>5</sub>-C<sub>7</sub> fused  
ring to the benzene ring (Ring III);

R<sup>5</sup>, R<sup>6</sup>, and R<sup>7</sup> each independently represents H, -CF<sub>3</sub>,  
-COR<sup>10</sup>, alkyl or aryl, said alkyl or aryl optionally being substituted  
with -OR<sup>10</sup>, -SR<sup>10</sup>, -S(O)<sub>t</sub>R<sup>11</sup>, -NR<sup>10</sup>COOR<sup>11</sup>, -N(R<sup>10</sup>)<sub>2</sub>, -NO<sub>2</sub>,

$-\text{COR}^{10}$ ,  $-\text{OCOR}^{10}$ ,  $-\text{OCO}_2\text{R}^{11}$ ,  $-\text{CO}_2\text{R}^{10}$ ,  $\text{OPO}_3\text{R}^{10}$ , or  $\text{R}^5$  is combined with  $\text{R}^6$  to represent  $=\text{O}$  or  $=\text{S}$ ; provided that for the groups  $-\text{OR}^{10}$ ,  $-\text{SR}^{10}$ , and  $-\text{N}(\text{R}^{10})_2$   $\text{R}^{10}$  is not H;

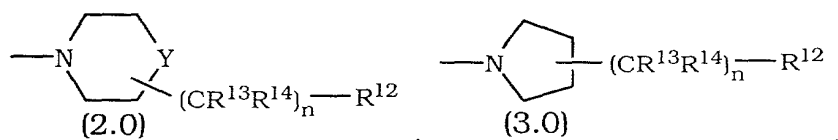
$\text{R}^{10}$  represents H, alkyl, aryl, or aralkyl;

5  $\text{R}^{11}$  represents alkyl or aryl;

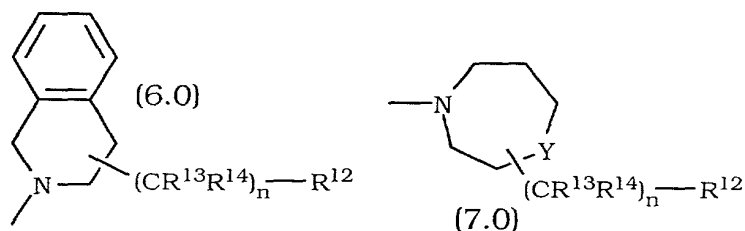
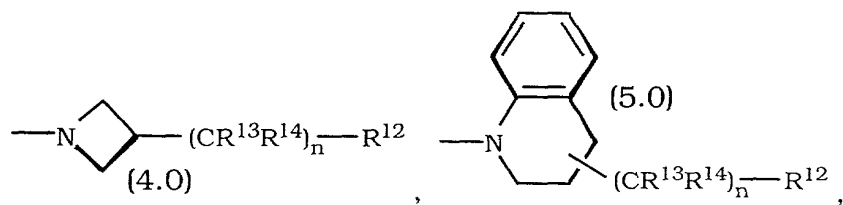
X represents N, CH or C, and when X is C the optional bond (represented by the dotted line) to carbon atom 11 is present, and when X is CH the optional bond (represented by the dotted line) to carbon atom 11 is absent;

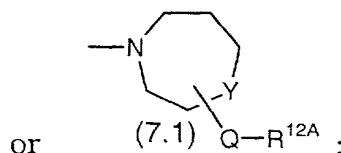
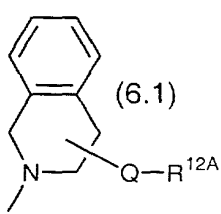
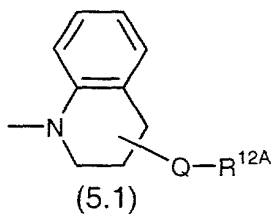
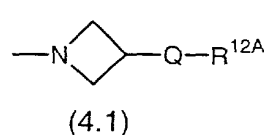
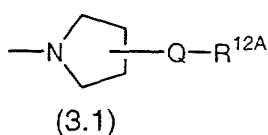
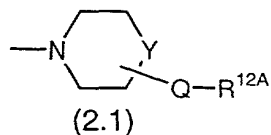
10 the dotted line between carbon atoms 5 and 6 represents an optional bond, such that when a double bond is present, A and B independently represent  $-\text{R}^{10}$ , halo,  $-\text{OR}^{11}$ ,  $-\text{OCO}_2\text{R}^{11}$  or  $-\text{OC}(\text{O})\text{R}^{10}$ , and when no double bond is present between carbon atoms 5 and 6, A and B each independently represent  $\text{H}_2$ ,  
 15  $-(\text{OR}^{11})_2$ , H and halo, dihalo, alkyl and H,  $(\text{alkyl})_2$ ,  $-\text{H}$  and  $-\text{OC}(\text{O})\text{R}^{10}$ , H and  $-\text{OR}^{10}$ ,  $=\text{O}$ , aryl and H,  $=\text{NOR}^{10}$  or  $-\text{O}-(\text{CH}_2)_p-\text{O}-$  wherein p is 2, 3 or 4;

$\text{R}^8$  represents a heterocyclic ring selected from:



20





said heterocyclic rings (2.0 to 7.0 and 2.1 to 7.1) being optionally substituted with one or more substituents independently selected from:

(a) alkyl,

(b) substituted alkyl wherein said substituents are selected from: halo, aryl,  $-OR^{15}$  or  $-N(R^{15})_2$ , heteroaryl,

heterocycloalkyl, cycloalkyl, wherein each  $R^{15}$  group is the same or different, provided that said optional substituent is not bound to a carbon atom that is adjacent to an oxygen or nitrogen atom, and wherein  $R^{15}$  is selected from : H, alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, or cycloalkylalkyl;

(c) hydroxyl, with the proviso that carbon atoms adjacent to the nitrogen, sulfur or oxygen atoms of the ring are not substituted with hydroxyl;

(d) alkyloxy or

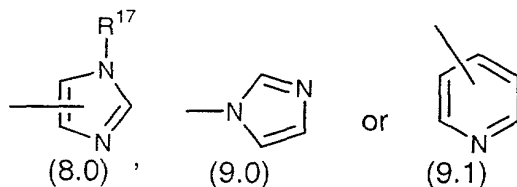
(e) arylalkyloxy;

Y represents  $CH_2$ ,  $NR^{16}$ , O, S, SO, or  $SO_2$  wherein  $R^{16}$  is selected from: H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, acyl, aroyl, carbamoyl, carboxamido, alkylsulfonyl, arylsulfonyl, arylalkylsulfonyl, sulfonamido, alkylsulfonamido, arylsulfonamido and arylalkylsulfonamido;

n is 0 to 6 ;

Q represents O or N, provided that Q is not adjacent to a heteroatom in the heterocycloalkyl rings of 2.1, 3.1, 4.1, 5.1, 6.1 and 7.1;

R<sup>12</sup> is selected from:



wherein R<sup>17</sup> is selected from: (1) H, (2) alkyl, (3) aryl, (4) arylalkyl, (5) substituted arylalkyl wherein the substituents are selected from halo or CN, (6) -C(aryl)<sub>3</sub>, (7) cycloalkyl, (8) substituted alkyl (as defined above in (b)), or (9) cycloalkylalkyl;

R<sup>12A</sup> is selected from rings 8.0 or 9.1, defined above;

said imidazolyl ring 8.0 optionally being substituted with one or two substituents, said imidazole ring 9.0 optionally being substituted with 1-3 substituents, and said pyridyl ring 9.1

optionally being substituted with 1-4 substituents, wherein said optional substituents for rings 8.0, 9.0 and 9.1 are bound to the carbon atoms of said rings and are independently selected from:

-NHC(O)R<sup>15</sup>, -C(R<sup>18</sup>)<sub>2</sub>OR<sup>19</sup>, -OR<sup>15</sup>, -SR<sup>15</sup>, F, Cl, Br, alkyl, substituted alkyl (as defined above in (b)), aryl, arylalkyl, cycloalkyl, or -N(R<sup>15</sup>)<sub>2</sub>; R<sup>15</sup> is as defined above; each R<sup>18</sup> is independently selected from H or alkyl; R<sup>19</sup> is selected from H or -C(O)NHR<sup>20</sup>, and R<sup>20</sup> is as defined below;

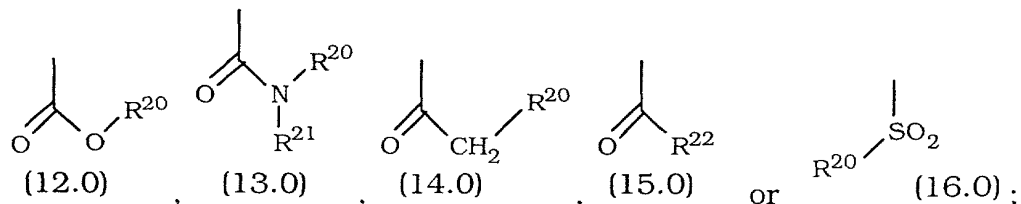
R<sup>13</sup> and R<sup>14</sup> for each n are independently selected from: H, F, alkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, cycloalkyl, cycloalkylalkyl or -CON(R<sup>15</sup>)<sub>2</sub> (wherein R<sup>15</sup> is as defined above),

-OR<sup>15</sup> or -N(R<sup>15</sup>)<sub>2</sub> provided that the -OR<sup>15</sup> and -N(R<sup>15</sup>)<sub>2</sub> groups are not bound to a carbon atom that is adjacent to a nitrogen atom, and provided that there can be only one -OH group on each carbon; and the substitutable R<sup>13</sup> and R<sup>14</sup> groups are optionally substituted with one or more substituents selected from: F, alkyl, cycloalkyl,

arylalkyl, or heteroarylalkyl; or

$R^{13}$  and  $R^{14}$ , for each n, together with the carbon atom to which they are bound, form a  $C_3$  to  $C_6$  cycloalkyl ring;

$R^9$  is selected from:



- 5  $R^{20}$  is selected from: H, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl, or heterocycloalkylalkyl, provided that  $R^{20}$  is not H when  $R^9$  is group 12.0 or 16.0;

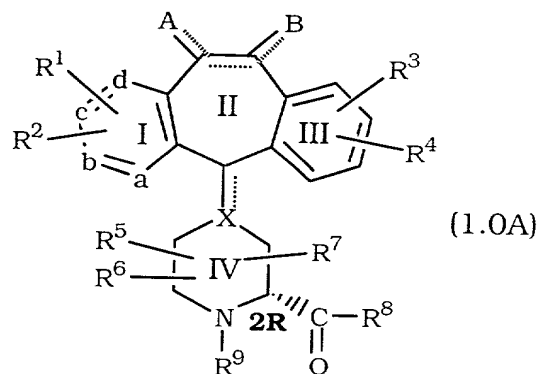
- 10 when  $R^{20}$  is other than H, then said  $R^{20}$  group is optionally substituted with one or more substituents selected from: halo, alkyl, aryl,  $-\text{OC}(\text{O})\text{R}^{15}$ ,  $-\text{OR}^{15}$  or  $-\text{N}(\text{R}^{15})_2$ , wherein each  $R^{15}$  group is the same or different, and wherein  $R^{15}$  is as defined above, provided that said optional substituent is not bound to a carbon atom that is adjacent to an oxygen or nitrogen atom;

- 15  $R^{21}$  is selected from: H, alkyl, aryl, arylalkyl, cycloalkyl, cycloalkylalkyl, heteroaryl, heteroarylalkyl, heterocycloalkyl or heterocycloalkylalkyl;

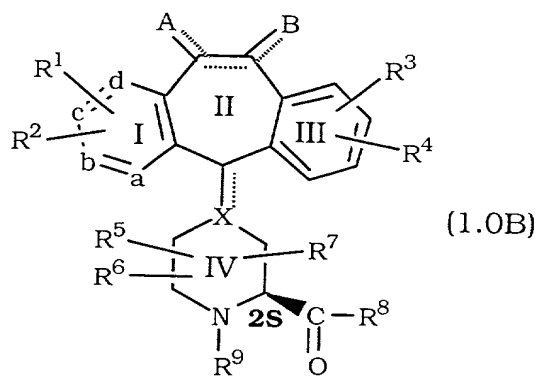
- 20 when  $R^{21}$  is other than H, then said  $R^{21}$  group is optionally substituted with one or more substituents selected from: alkyl, aryl, wherein each  $R^{15}$  group is the same or different, and wherein  $R^{15}$  is as defined above; and

$R^{22}$  is selected from cycloalkyl, heterocycloalkyl, aryl, substituted aryl, alkyl, substituted alkyl or substituted cycloalkyl.

2. The compound of Claim 1 having the structure



3. The compound of Claim 1 having the structure:



4. The compound of Claim 1 wherein  $R^1$  to  $R^4$  is independently selected from H, Br, F or Cl;  $R^5$  to  $R^7$  is H; a is N and the remaining b, c and d substituents are carbon; A and B are  $H_2$ ; and n is 1 to 3.

5. The compound of Claim 1 wherein  $R^1$  to  $R^4$  is independently selected from H, Br, F or Cl;  $R^5$  to  $R^7$  is H; a, b, c and d are carbon; A and B are  $H_2$ ; n is 1 to 3.

6. The compound of Claim 1 wherein  $R^8$  is ring 2.0 and the  $-(CR^{13}R^{14})_n-R^{12}$  substituent is in the 2- or 3- position.

7. The compound of Claim 1 wherein  $R^8$  is ring 2.0 and the  $-(CR^{13}R^{14})_n-R^{12}$  substituent is in the 2- or 3- position, and Y is  $CH_2$ .

8. The compound of claim 1 wherein  $R^{13}$  and  $R^{14}$  are H.

9. The compound of Claim 1 wherein Y is selected from S, SO, or SO<sub>2</sub>.

5

10. The compound of Claim 1 wherein Y is O.

11. The compound of Claim 1 wherein Y is NR<sup>16</sup>.

10

12. The compound of Claim 1 wherein R<sup>9</sup> is group 12.0.

13. The compound of Claim 1 wherein R<sup>9</sup> is group 13.0.

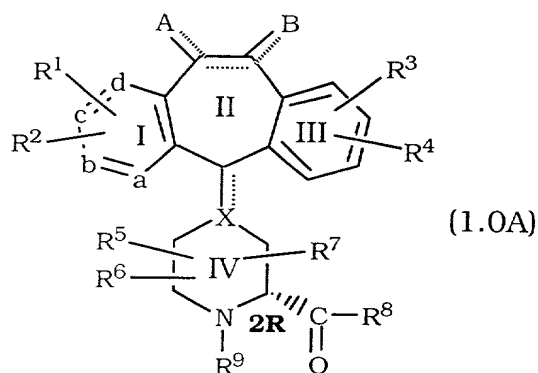
14. The compound of Claim 1 wherein R<sup>9</sup> is group 15.0.

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15. The compound of Claim 1 wherein R<sup>1</sup> to R<sup>4</sup> is independently selected from H, Br, F or Cl; R<sup>5</sup> to R<sup>7</sup> is H, a is N and the remaining b, c and d substituents are carbon; A and B are H<sub>2</sub>; and n is 1 to 3; R<sup>8</sup> is ring 2.0 and the  $-(CR^{13}R^{14})_n-R^{12}$  substituent is in the 2- or 3- position, and Y is CH<sub>2</sub>.

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16. The compound of Claim 15 having the structure:



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17. The compound of Claim 16 wherein  $R^{13}$  and  $R^{14}$  are H.

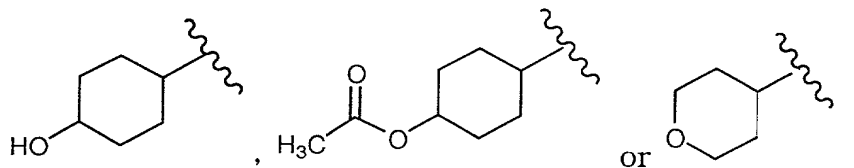
18. The compound of Claim 17 wherein  $R^{12}$  is 9.0.

19. The compound of Claim 17 wherein  $R^9$  is 12.0.

5 20. The compound of Claim 17 wherein  $R^9$  is 13.0.

21. The compound of Claim 17 wherein  $R^9$  is 15.0.

10 22. The compound of Claim 17 wherein  $R^{20}$  is selected from t-butyl, i-propyl, neopentyl, cyclohexyl, cyclopropylmethyl,



15 23. The compound of Claim 16 wherein  $R^9$  is selected from 12.0 or 13.0, and wherein  $R^{21}$  for 13.0 is H.

20 24. The compound of Claim 1 selected from a compound of Examples 1-4, 4.1, 4.2, 10-19, 24-51, 74, 138, 142, 144, 145, 35(A), 35(C), 35(D), 35(E), 35(F), 41(A), 41(B), 41(C), 47(A), 47(B), 47(D), 47(G), 47(H), 47(I), 47(K), 47(L), 47(M), 47(N), 47(O), 47(P), 47(R), 47(S), 47(T), 47(U), 47(CC), 51(A) to 51 (D), 138 A to 147A, 148 to 158, 160, 161, 163, 169 to 180, 183 to 188, 191, 192, 197, 201, 207 to 216, 227 to 234, 238 to 240, 245, 255 to 262, 287 to 294, 297 to 303, 316 to 324, 351 to 354, 383, 384, 387, 388, 391, 392, 394 to 397, 407, 408, 409, 410, 411, 412, 414, 415 to 417, 25 419, 422 or 424.

30 25. The compound of Claim 1 selected from a compound of Examples 35(C), 41(A), 47(S), 47(T), 140A, 144 isomer 1, 144 isomer 2, 163, 164, 183, 185, 215, 238, 258, 259, 287, 291, 292, 298, 300, 320, 351, 353, 411 or 416.



26. The compound of Claim 1 selected from a compound of Examples 47(A) or 140A.

27. A method of treating tumor cells comprising  
5 administering an effective amount of a compound of Claim 1.

28. The method of Claim 27 wherein the tumor cells treated are pancreatic tumor cells, lung cancer cells, myeloid leukemia tumor cells, thyroid follicular tumor cells, myelodysplastic tumor  
10 cells, epidermal carcinoma tumor cells, bladder carcinoma tumor cells, colon tumors cells, melanoma, breast tumor cells and prostate tumor cells.

29. A method of treating tumor cells wherein the Ras  
15 protein is activated as a result of oncogenic mutation in genes other than the Ras gene, comprising administering an effective amount of a compound of Claim 1.

30. A method of inhibiting farnesyl protein transferase  
20 comprising the administration of an effective amount of the compound of Claim 1.

31. A pharmaceutical composition for inhibiting farnesyl protein transferase comprising an effective amount of compound of  
25 Claim 1 in combination with a pharmaceutically acceptable carrier.

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